REMARKS/ARGUMENTS

Claims 19-28, 30 and 32-44 are active in the case. Reconsideration is respectfully requested.

Applicants' representative wishes to thank Examiner Haghighatian for the helpful and courteous interview of August 7, 2008 concerning the issues in the above-identified application. As a result of the discussion, it is believed that the issues have been clarified and that the prosecution of the application has been materially advanced.

The present invention relates to a process of preparing an aqueous suspension of drug particles to be administered to a subject by inhalation.

Prior Art Rejection, 35 USC 103

Claims 19-28, 30 and 32-44 stand rejected based on 35 USC 103 as obvious over Bernini et al, WO 00/25746. This ground of rejection is respectfully traversed.

As applicants' representative stated at the interview, the background context of the present invention is found in the process described in the '746 reference. That is, '746 describes a process of preparing an aqueous suspension of a micronized active ingredient, wherein the starting material such as BDP is added to the turboemulsifier from the top of the turboemulsifier at atmospheric pressure. A disadvantage of this procedure is that a long processing time is required in order to disperse the active ingredient in a sterile solution. Also, the suspension that is obtained does not meet the requirement of homogeneity of the micronized product in a satisfactory manner. A claimed modification of the conventional process is to conduct the dispersion process under an atmosphere of elevated pressure, which achieves a significant improvement in the micronization of the dispersed solid material. This is shown by the data in Table 6 of the reference which demonstrate that when the suspension process is conducted under a pressure of over 500 bar, the sizes of particles of

beclomethasone dipropionate (BDP) obtained are significantly reduced (38 %) from 8.73 to 5.42 μm at a median volumetric diameter of 90 %. A further reduction of particle size of 6.5 % (5.42 μm to 5.07 μm) is observed at a median volumetric diameter of 90 %. The discovery of the present invention, on the other hand. is that, if in the loading of active ingredient into the turboemulsifier, the loading occurs by way of the aqueous solution through the turbine component of the emulsifier rather than from the top of the device at atmospheric pressure as done in the process disclosed in the '746 reference, it is possible to achieve a far more efficient dispersal of active ingredient, and therefore it is possible to prepare homogeneous suspensions with a distribution profile that is reproducible from one batch to the other, in a much shorter time. In addition, because the micronized active ingredient is passed through the turbine under vacuum, it is possible to obtain finer particles, inside the emulsifier, that have a narrower, more homogenous particle size distribution range with no further need for additional treatments such as the high pressure homogenizer described in '746. In fact, the '746 does not show or suggest a modification of the turboemulsifier process in which particles of active ingredient are fed into the emulsifying device through the turbine.

In order to demonstrate the effectiveness of the "through the turbine processing" of an active ingredient by the present method, applicants refer to the data in Table 2 of Example 3 of the present specification. The micronized product of Example 2 involving particles of BDP is described in Example 2. The data in the column marked Prep 1 are obtained from the product of Example 2 of the application. For the three product categories at the 90 % median volumetric diameter level, the size of particles is less than 8 microns and that at the level of at least 50 % the size of particles is within the range of 2 to 3.5 microns. In the column entitled Prep 2, the data presented were obtained by an experiment within the scope of the method of the '746 reference. It is clear that at the median volumetric diameter of 90 % the particle size values obtained are well in excess of the 8 micron particle size limitation of the present claim.

These contrasting results in Table 2 confirm that the process of the present invention produces finer particles with a narrower and more homogeneous particle-size distribution. These results are of commercial significance.

Double Patenting

Claims 19-28, 30 and 32-44 stand rejected based on the ground of non-statutory obviousness-type double patenting over Claims 2-9 and 13 of U.S. Patent 6,464,958. This ground of rejection is respectfully traversed.

As Applicants have stated above, the gist of the present process as claimed is the mode of entry of particulate active ingredient into a turboemulsifier by way of the vacuum which is generated at the turbine component of the device. On the other hand, the claims of the '958 reference, although claiming a method of preparing an aerosol inhalable suspension of particles in a turboemulsifier, does not suggest a modification of the method in which a vacuum is applied to the emulsifier device through the turbine at the bottom of the turboemulsifier. The difference the procedure of the present invention makes on the particle sizes of an active ingredient and the distribution of particles has been clearly discussed above. Accordingly, the obviousness ground of rejection is overcome and withdrawal of the rejection is respectfully requested.

Claims 9-42 stand provisionally rejected based on the ground of non-statutory obviousness-type double patenting over Claims 1-20 of U.S. Patent Publication 2007/0140980. This ground of rejection is respectfully traversed.

The claimed process of the publication is the preparation of a sterile formulation in the form of an aqueous suspension for pulmonary administration by inhalation. The process is accomplished by the preparation of a sterile drug or active agent containing solution by filtration and separately a sterile aqueous phase containing excipients in a turboemulsifier

followed by mixture of the two mediums and removal of the organic solvent to form the sterilized aqueous drug product. There is absolutely no suggestion in the claims of the use of a turboemulsifier alone that contains an aqueous drug or active agent containing medium, whereby the application of a vacuum through the turbine at the base of the turboemulsifier accomplishes the micronization of the particles of active ingredient in the aqueous medium to size ranges very favorable for the preparation of a therapeutic product having favorable inhalation characteristics. None of the process steps of present Claim 19 are found in the process claim of the publication. Accordingly, the present invention as claimed is patentable over the claims of the reference and withdrawal of the rejection is respectfully requested.

It is believed that the application is in proper condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

Frederick D. Vastine, Ph.D.
Registration No. 27,013

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 06/04)